Introduction to the Age and Ageing Sarcopenia collection

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Sarcopenia – the loss of skeletal muscle mass and function that accompanies ageing – is now an established pathophysiological entity. There is increasing appreciation of its importance, and a growing, although incomplete, understanding of its causes. It is closely linked to physical frailty, and we are now at a point where detection of sarcopenia is beginning to be incorporated into clinical practice, and where potential interventions are beginning to undergo large clinical trials.

The on-line *Age and Ageing* collection of sarcopenia papers is therefore timely. We have selected key references that showcase how *Age and Ageing* has been involved in the development of the field, how definitions of sarcopenia have evolved, evidence on the prevalence, causes, and adverse effects of sarcopenia, as well as reviews of current therapy and insights into how the field might evolve in future. We hope that the collection will give readers not only an overview of the current state of the art, but a sense of how far we have travelled in sarcopenia research over the last few decades. The collection, including details of all the references are available on-line at [insert web address here]

Beginnings and progress

Long before the concept of sarcopenia had acquired its current label, Maclennan and colleagues described the reduction in grip strength with increasing age, and noted only a marginal decrease in muscle mass. These two components of sarcopenia continue to be the focus of debate within the field – which is most important, which should be the target for interventions to improve, and do we really need to measure both in clinical practice?

Further work over the next few years cemented the important relationships between muscle function and clinical outcomes. Hyatt and colleagues showed that muscle strength was independently associated with activities of daily living and the need for care. Studies such as this provided the intellectual underpinning that led to increased interest in muscle function from the academic geriatric medicine community over the last twenty five years.

The paper that perhaps did more than any other to put sarcopenia on the map as a clinical entity, not just for researchers but for practitioners, was the 2010 European Working Group consensus

statement. This paper provided easily accessible information on what sarcopenia is, diagnostic criteria, and diagnostic methods. It rapidly became the most highly-cited paper in Age and Ageing's history (1500 and counting!), and remains a cornerstone reference within the field. The huge number of downloads (over 60,000 at the time of writing) for this paper is testament to both its importance to researchers and its relevance to clinicians.

Definitions and prevalence

Sarcopenia prevalence is closely related to the choice of definition, and increases with age; in the BELFRAIL study by Legrand and colleagues, 12.5% of those age 80 and over were sarcopenic by the European Working Group definition. Even in the young old, such as participants in the Hertfordshire Cohort Study reported by Patel and colleagues, sarcopenia was not uncommon, affecting between 4.6 and 7.9% depending on gender and definition. Sarcopenia is a global problem, but different definitions may be appropriate for different populations. Dodds recent meta-analysis suggests that cut-offs for defining sarcopenia in developing country populations may need to be substantially different from those in western nations.

Causes and consequences

The pathophysiology of sarcopenia is complex, and not yet fully elucidated. Cesari and colleagues showed only a weak association between sarcopenia measures and endurance exercise capacity in patients with COPD, reminding us that sarcopenia is but one type of skeletal muscle dysfunction seen in older people. Diseases such as COPD and heart failure bring their own skeletal myopathies, and there may well be subtypes within the umbrella definition of sarcopenia yet to discover as well. There is plenty to find out still about the antecedents of sarcopenia. Cohorts with long follow-up periods are now giving us insight into the natural history of sarcopenia, as shown by 20 years of longitudinal data from Sweden reported by Sternang and colleagues.

Sarcopenia is linked to a number of adverse health outcomes. We now know that it is not only associated with falls, impaired activities of daily living, and the need for institutional care; sarcopenia is also associated with an earlier death. Data from the ilSIRENTE study found that sarcopenia was associated with more than double the hazard ratio for death after adjustment for confounders. Kerr and colleagues examined the relationship between grip strength and likelihood of discharge home in patients already in hospital; every 1Kg decrease in grip strength was associated with a 3% decrease in

the chance of being discharged home. As the authors point out, such data make it surprising that grip strength has not yet been taken up into clinical practice more widely.

Measuring muscle function in multiple areas of the body might help with our ability to predict outcomes including mortality and hospitalisation; the Toledo cohort found that patterns of muscle weakness associated with these outcomes were different in men and women, and that weakness in multiple areas of the body improved prediction. Not every adverse event in old age is attributable to sarcopenia however; data from the EPIDOS cohort found no association between cognitive impairment and sarcopenia.

Interventions

To date, there have been relatively few randomised controlled trials to treat sarcopenia, although this is starting to change. In a 2004 systematic review, Borst reviewed the evidence around resistance training, testosterone and growth hormone. Even at this relatively early stage in our understanding, resistance training had clear evidence of a beneficial effect in sarcopenia. An updated review from the International Sarcopenia Initiative in 2014 confirmed the benefits of resistance training, but also suggested that essential amino acids (particularly leucine) might also have beneficial effects. Larger trials will confirm or refute this finding over the next few years.

Where to next?

There remains much to be done, but the future almost certainly lies in embedding sarcopenia diagnosis into clinical practice, in a better understanding of the pathophysiology of the condition, and in testing and implementing interventions to prevent or treat sarcopenia. Ensuring patient-centred outcome measures are used in trials is a key concern; it is not sufficient merely to show an improvement in muscle strength or mass, and the derivation of a disease-specific quality of life measure (SarQoL) is a recent example of a tool that may help with this. The state of the art and future direction of the field is captured well in a recent New Horizons article by Sayer and colleagues.

Conclusions

The papers in the collection are chosen to both illustrate the evolution of concepts and knowledge in the field of sarcopenia, but also to showcase the breadth of current research, and to highlight the current state of the field. We are at an important juncture in the sarcopenia story, where research findings begin to cross over to influence clinical practice. The articles selected showcase the contribution made by *Age and Ageing* to this field, and we anticipate that the journal will continue to

be a leading forum for disseminating knowledge in sarcopenia research and practice in the coming years.